# PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
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# PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

| | |
|---|---|
| Date of mailing (*day/month/year*) | 18 NOV 2005 |
| Applicant's or agent's file reference<br>91830/0530186 | FOR FURTHER ACTION<br>See paragraph 2 below |

| International application No. | International filing date (*day/month/year*) | Priority date (*day/month/year*) |
|---|---|---|
| PCT/US04/42949 | 20 December 2004 (20.12.2004) | 19 December 2003 (19.12.2003) |

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A01N 43/04; A61K 31/70; C07H 21/04 and US Cl.: 514/44; 536/24.1, 24.5

Applicant

UNIVERSITY OF CINCINNATI

1. This opinion contains indications relating to the following items:

- [x] Box No. I — Basis of the opinion
- [ ] Box No. II — Priority
- [ ] Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- [ ] Box No. IV — Lack of unity of invention
- [x] Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- [ ] Box No. VI — Certain documents cited
- [ ] Box No. VII — Certain defects in the international application
- [ ] Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| Name and mailing address of the ISA/US | Date of completion of this opinion | Authorized officer |
|---|---|---|
| Mail Stop PCT, Attn: ISA/US<br>Commissioner for Patents<br>P.O. Box 1450<br>Alexandria, Virginia 22313-1450<br>Facsimile No. (703) 305-3230 | 03 September 2005 (03.09.2005) | Janet L. Epps-Ford, Ph.D.<br>Telephone No. 571-272-0547 |

Form PCT/ISA/237 (cover sheet) (April 2005)

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/42949

**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No. PCT/US04/42949

**Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | |
|---|---|---|
| Novelty (N) | Claims 10-29 | YES |
| | Claims 1-9 | NO |
| Inventive step (IS) | Claims 1-29 | YES |
| | Claims NONE | NO |
| Industrial applicability (IA) | Claims 1-29 | YES |
| | Claims NONE | NO |

2. Citations and explanations:

Claims 1-3, 5-9 lack novelty under PCT Article 33(2) as being anticipated by Morishita et al. (EP1362600A1), Tanaka et al. or Dzau et al.

Claim 1 is drawn to a concatemerized double-stranded oligonucleotide molecule comprising at least two copies of a nucleotide sequence comprising a sequence or sequences that act as transcription factor decoys.

Morishita et al. describes compositions comprising at least one decoy and a pharmaceutically acceptable carrier. The at least one decoy of Morishita et al. may comprise an oligonucleotide including at least two decoys bonded to each other, the at least two decoys being selected from the group consisting of an NF-kB decoy, a STAT-1 decoy, a GATA-3 decoy, a STAT-6 decoy, an AP-1 decoy and an ETS decoy. See claims 1-3 of this reference. Additionally, Morishita et al. teach that the compositions can be used to treat inflammatory disorders such as atopic dermatitis, psoriasis, ulcerative colitis, and Chron's disease.

On pages 3069-3070 Tanaka et al. disclose multiple oligonucleotides that comprise at least two repeated sequences in the same oligonucleotide, wherein the sequences are recognized by the NFkB transcription factor.

Dzau et al. teach a decoy comprising two E2F binding sites in one double stranded molecule. (see page 5.

Claims 1-3, and 5-29 lack an inventive step under PCT Article 33(3) as being obvious over Morishita et al. (EP1362600A1), in view of Tanaka et al. or Morishita et al. (EP 1362600A1).
Morishita et al. (EP0824918A1) teach the use of NFkB decoys for the treatment of ischemic diseases, inflammatory diseases, autoimmune diseases, cancer metastasis, and cachexia, post-PTCA restenosis, and reperfusion disorders (see claims).

Morishita et al. (EP0824918A1), does not teach decoys comprising at least two binding sites.

The teachings of Tanaka et al. and Morishita et al. (EP 1362600A1) as set forth above is included herein.

The prior art teaches the effectiveness of decoys comprising two transcription factor binding regions, and in particular NFkB binding sites, and the prior art teach the treatment of various disorders with NFkB decoys. Therefore, the ordinary skilled artisan would have been motivated to modify the teachings of Morishita et al. (EP0824918A1) with the teachings of Morishita et al. (EP 1362600A1) or Tanaka et al. to use the NFkB decoys comprising at least two binding sites for NFkB, because it would have been obvious to substitute one functionally equivalent inhibitor of NFkB activity with another, with the expectation of producing the same results, or improved results since the concatamer decoys bind more NFkB.